

PLASMA ENDOCANNABINOID ALTERATIONS AS A LINK IN THE COMORBIDITY OF ALZHEIMER'S DISEASE AND TYPE 2 DIABETES MELLITUS

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Over the last several years, studies have implied the role of endocannabinoids like 2-AG and 2-OG in the impairment of β -cell function and insulin secretion, as well as the control of lipid and glucose metabolism in the periphery. Besides, alterations in the endocannabinidiome are associated with the development of dementia. Since type 2 diabetes mellitus (T2DM) is an established risk factor for late-life cognitive decline, we sought to evaluate the possible link between the alterations in plasma endocannabinoids as possible biomarkers of cognitive decline in elder patients with T2DM.

In the present study, we evaluated the plasma levels of endocannabinoids in a cohort of elder controls and patients suffering from T2DM, with either mild cognitive impairment (MCI) or Alzheimer's disease (AD). These patients were evaluated for cognitive performance at the beginning of the study and their regional brain metabolic activity was assessed by PET-¹⁸FDG. We found that T2DM patients showed decreased levels of brain metabolic activity as determined by PET-¹⁸FDG in the inferior parietal lobe, caudate, and thalamus, which were decreased and related to poor cognitive performance shown by both BLESSED and MMSE tests. Segregation of patients based on their cognitive status (MCI or AD) showed basal lower metabolism in the aforementioned regions, which was exacerbated in patients with AD and T2DM comorbidity. Correlation analysis showed plasma levels of endocannabinoids 2-AG, 2-LG, and 2-OG were inversely related to brain metabolism in these areas, as well as being related to worse scores by the BLESSED and MMSE tests.

Our results depict that plasma endocannabinoids are potential biomarkers linking the development of cognitive decline with the occurrence of T2DM.

Keywords: endocannabinoid, biomarkers, diabetes mellitus, mild cognitive impairment

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